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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,110	03/07/2001	James Leushner	VGEN.P-058-2	5580

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,110	LEUSHNER ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. Applicant amendment filed on October 20, 2003 is acknowledged. Claims 13-36 are pending. All of the amendments and arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made Final.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejections under 102 directed to claims 13-16, 25-28 as being anticipated by Jordon et al. are maintained and discussed below. The prior art rejections directed to claims 13, 14, 16, 25, 26 and 28 as being anticipated by Vasta et al are maintained and discussed below. The prior art rejection directed to claims 17-24 and 29-36 as being obvious over Ruano in view of Rao and further in view of Ahern are being maintained and discussed below.

Claim Rejections - 35 USC § 102

4. Once again, claims 13-16, 25-28 rejected under 35 U.S.C. 102(e) as being anticipated by Jordan (6,017,699, filed March 29, 1996). Regarding claims 13-16, and 25-28, Jordan teaches a kit consisting of, in package combination, region-specific reagents for a genomic DNA sample of a microorganism (col. 6, lines 55 to col. 7, line 4), wherein the region-specific reagents comprises a pair of primers which binds to the sense (coding) and antisense (noncoding) strands (col. 10, lines 7-17). The reference do not expressly state that the primers flank the target DNA regions within the genomic microorganism's DNA. However, this is deemed inherent in the teaching of the construction of the set of species-specific primers for PCR

amplification (col. 5, lines 7-17 and Example 4 in it's entirety). Likewise it is commonly known in the art that in PCR amplification reactions, primers that bind to the sense and antisense strands of the target DNA sample also flank the target region to be amplified. Therefore, Jordan meets the limitations of claims 13-16 and 25-28.

Applicant's traversal

5. Applicant's traverses the rejections on the following grounds: Applicant recites claim 13 and states that "the examiner has not taken into account the highlight words "**a single tube**" of region-specific reagents for each DNA region to be sequenced". Applicant contends that the examiner cites "that the reference of Jordan teaches "a kit consisting of, in package combination, region specific reagents". Applicant states that "thus, the Examiner's characterization of the reference does not meet the limitations of the claims". Applicant states that "there is no teaching in the reference that all of the region specific reagents are in a single tube and indeed this would not make sense since the Jordan patent teaches performing two types of tests, one with hybridization probes and one by PCR fragments analysis". Applicant concludes that there can be no anticipation.

Examiner's Response

6. Applicant's arguments have been thoroughly review and considered but they are not found persuasive for the reasons that follows: Firstly, the courts have established that during patent examination, the claims must be interpreted broadly as reasonably allow *(In re Zletz, 893 F.2d321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989)*. In this case, the limitations "said kit consisting of, in package combination, a single tube of region-specific reagents for each DNA region to be sequence..." can broadly be interpreted as the region-specific reagents each being in a separate container or tube or all the reagents together being in a separate container or tube or being packaged in combination together in a box, container, tube or etc. Likewise, the specification does not specifically define the kit as having all the region specific reagents in a single tube or specifically specify that a single tube is required for or is

necessary for the region specific reagents of the kit. Therefore, contrary to Applicant's arguments the reference of Jordon et al. meets the limitations of the claimed invention. The reference of Jordon et al teaches that "for convenience, all of the necessary reagents for sequencing are "packaged in combination" in the kit". Thus implying that the reagents of the kit are packaged together in a single tube or box or container or etc as required by the claim. The use of a tube or container or box is inherently implied in the teaching of Jordan. Secondly, Applicant's arguments do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Specifically because "kits having a single tube or single container of packaged reagents " is well known in the prior art. Therefore, in view of the foregoing, the rejection under 35 USC 102 is maintained.

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7. Once again, claims 13, 14, 16, 25-26, 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Vasta et al. (6,326,485, effective filing date July 26 1996). Regarding claims 13, 14, 16, 25-26 and 28, Vasta et al. discloses a kit consisting of, in a single container a region-specific reagent for a DNA region, wherein said region-specific reagents comprises a pair of primers which binds to the sense and antisense strands and flank the region of microorganism DNA (col. 12, lines 54-67 to col. 13, lines 4; see also col. 8, lines 30-34 and lines 65-67). Therefore, Vasta et al. meet the limitations of claims 13, 14, 16, 25-26 and 28.

Applicant's Traversal

8. Applicant traverses the rejection on the following grounds: Applicant states that "the examiner states that the reference states that the reference discloses a kit consisting of a single container". Applicant states that there is no instance in the Vasta patent wherein the patent actually makes such a disclosure. Applicant states that Vasta does disclose a kit, and states that the "kit comprises a container having a pair of outwardly directed PCR primers to the NTS region of the microorganism(s) being tested

for". Applicant states that this does not say that the kit consists of a single tube or region specific reagents for each DNA region to be sequence. Applicant concludes that therefore, there is no anticipation.

Examiner's Response

9. Applicant's arguments submitted on October 20, 2003 have been fully considered but they are not found persuasive for the reasons that follows: As noted above, the courts have established that during patent examination, the claims must be interpreted broadly as reasonably allow *(In re Zletz, 893 F.2d321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989)*. In this case, the limitations "said kit consisting of, in package combination, a single tube of region-specific reagents for each DNA region to be sequence..." can broadly be interpreted as the region-specific reagents each being in a separate container or tube or all the reagents together being in a separate container or tube or being packaged in combination together in a box, container, tube or etc. Likewise, the specification does not specifically define the kit as having all the region specific reagents in a single tube or specifically specify that a single tube is required for or is necessary for the region specific reagents of the kit. Additionally, the specification does specifically provide a limitation as to what is considered "regions specific reagents". Therefore, one of ordinary skill in the art can simply interpret "region-specific reagents" as "primers for a particular region". Contrary to Applicant's arguments the reference of Vasta et al. meets the limitations of the claimed invention because the reference teaches wherein in a single container, a pair of primers for the NTS region of the microorganism(s) being tested for (region specific reagents) are packaged together. The reference further teaches that single container will further contain necessary buffers, enzymes and etc. Therefore, the instant claims as broadly written are anticipated by Vasta et al. Additionally as stated above, Applicant's arguments do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made because "kits having a single tube or single container of packaged reagents" is well known in the prior art. Therefore, in view of the foregoing, the rejection under 35 USC 102 is maintained.

Claim Rejections - 35 USC § 103

10. Once again, claims 17-24 and 29-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano (5,427,911, (patent date June 27, 1995) in view of Rao (Analytical Biochemistry, vol. 216, pages 1-14, (1994) and further in view of Ahern (The Scientist, Vol. 9, No. 15, pages 1-15, June 1995). Regarding claims 17-24 and 29-36, Rao et al. teach a method for sequencing genomic DNA sample, the method comprising amplifying in vitro with two locus specific primers that flank both ends of the target region to obtain a template, synthesizing simultaneously truncated strands from both ends of the template by introducing a dideoxynucleotide terminator for each of the four bases adenine, guanine, cytosine and thymine and introducing a label or labels specific for either or both of the 5' ends of the synthesizing strands, thermally cycling steps to provide a sufficiently readable signal (col. 2, lines 3-23). Ruano further teaches wherein the dideoynucleotide triphosphate is in a mole ratio of about 1:10 to the corresponding deoxynucleotide triphosphate (col. 6, lines 47-68).

The reference of Ruano differs from the instant invention in that the reference does not teach wherein the method comprises the dideoxynucleotide triphosphate in a mole ratio of 1:50 to 1: 1000 or in a mole ratio of 1:1000 to 1: 500 to the corresponding deoxynucleotide triphosphates. Ruano also does not teach wherein the components of the method of sequencing are in the form of a kit.

In a method similar to that of Ruano, Rao teaches a method of direct sequencing of polymerase chain reaction-amplified DNA. Rao teaches wherein the method comprises mixing the PCR-amplified genomic DNA, labeled primer sequencing buffer and Taq polymerase in a tube, adding to the mixture in four separate tubes, four dNTPs and at least one dideoxynucleotide triphosphate, perform thermal cycling (see Table 3, page 5). Rao differs from the instant invention in that Rao does not teach wherein the mole ratio of the ddNTP:dNTP is from 1:50 to 1:1000 or 1:100 to 1:500. Rao also does not teach wherein the polymerase enzyme incorporates dNTPs into an extending nucleic acid polymerase at a rate which is no less than 0.5 times the rate of incorporation of dNTPs. However, Rao discloses that the composition of the dNTP/ddNTP mix varies depending on the type of polymerase preparation used. Rao additionally

states that different polymerases require different dNTP/ddNTP ratios for optimal chain terminations and therefore,, the reagents or kits for one polymerase cannot be substituted with those for a different polymerase. Rao further teaches that optimal buffer conditions for the synthesizing reaction will vary based on the specific DNA polymerase used (see Table 3 legend).

3. In a review article Ahern teaches the advantages of a kit. Ahern teaches that a kit provides convenience, time management and ease of practicing to the investigator (page 4, second-forth paragraphs). Therefore in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have recognized that the mole ratio of reagents of the kit and polymerase extending ability may vary based on the chose of polymerase preparation used in the sequencing reaction and desired results as suggested by Rao. One of ordinary skill in the art at the time of the claimed invention would have been further motivated to have combined the components of the sequencing method as taught by Ruano and Rao in the form of a kit for the obvious benefits taught by Ahern that a kit provides convenience, time management and ease of practicing to the investigator.

Applicant's Traversal

11. Applicant traverses the rejection on the following ground: Applicant states that the Examiner has not mentioned the limitation of claim 13 on which the rejected claims ultimately depend, and in particular, has not mentioned the recitation in claim 13 that the kit consist of a single tube of region specific reagents for each region to be sequenced. Applicant contends that looking at Figure 5 of Ruano and the accompanying text in col. 6, particularly lines 34-38, it can be seen that Ruano does not disclose or suggest this limitation. Applicant states that the labeled primers, which are region specific tubes are placed in separate tubes. Applicant states that theses reagents must be in separate containers if they are to be used in this way, and therefore the limitations for claim 13 are not met. Applicant states that Rao does not offer anything further on this point. Applicant states that indeed Rao uses radiolabeled primers, all labeled with the same isotope. These must necessarily be kept separate because the labeled products cannot be distinguished. Applicant states that Ahern has no specific information on the contents of a kit

or the way in which is arranged, only that kits may be desirable. Applicant submits that the rejection should be withdrawn.

Examiner's Response

12. Applicant's amendment filed on October 20, 2003 has been fully considered but has not been found persuasive for the reasons that follows: As noted earlier, the claims as written are not limited in the way applicant contends. Likewise, the specification does not define or provide evidence that a single tube is required for all of the region specific reagents in the kit or that the reagents are not packaged separately or what actually constitutes a single tube of region specific reagents. Therefore, given the broadest interpretation of the claims, the limitation recited in claim 13 can merely mean that each region specific reagent such as e.g., primers, are packaged in a single container or tube or box or etc or can be packaged together as a whole in a single container or tube or box or etc. This limitation is found in the reference of Ruano. Ruano et al at col. 8, lines 3-12, teach that "the present invention encompasses kits for conducting the aforementioned processes." The reference states that such kits include in one (single) or more containers, a set of instructions, one or more of a thermally stable enzyme, salts, deoxynucleotides, dideoxynucleotides and labeled primers". The secondary reference of Rao teaches wherein in the region specific reagents are placed in a separate single tube, which is also encompassed by the claims and the tertiary reference of Ahern provides motivation for wanting all of the reagents in the form of a kit. Therefore, the limitations of the claims are met by the cited references. Likewise, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Finally, as noted above, Applicant's arguments do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made because "kits having a single tube or single container of packaged reagents" is well known in the prior art. Therefore, in view of the foregoing, the rejection under 35 USC 103 is maintained.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (703) 305-1680. After January 14, 2004, the examiner cam be reached at (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308 0196.

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

1/8/04